

## PAPERS

## Palliation of malignant dysphagia by ethanol induced tumour necrosis

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### Abstract

**Thirty two patients (74 (43–93) years; median, (range)) with dysphagia because of inoperable, unresectable or recurrent oesophagogastric carcinoma were treated by ethanol induced tumour necrosis (ETN). Endoscopic injection of absolute alcohol was performed using a variceal injector needle, with 0.5–1 ml aliquots injected retrogradely from distal to proximal tumour margin. Dilatation to 12 mm was used only if the endoscope would not traverse the stricture. In patients with total occlusion, injection into the proximal tumour was followed by a repeat endoscopy 3–7 days later. Dysphagia was graded from 0=no dysphagia to 4=total dysphagia. The significance of changes in the dysphagia grade after ETN were assessed using the Wilcoxon rank sum test. Results (median (range)) were as follows: stricture length=5.0 cm (1–15). Dysphagia grade before treatment was 3 (2–4) improving after first treatment to 1 (0–3),  $p<0.003$ . Best dysphagia grade achieved was 1 (0–3) and interval between treatments was 28.5 days (4–170). The volume of ethanol injected=10 ml (1.5–29) and survival after first treatment was 93 days (6–660). The number of treatment sessions required to achieve best grade=1 (1–3). There were no treatment complications. ETN significantly improves dysphagia. Results of palliation are similar to those of laser therapy, but can be achieved quickly and safely on a day case basis in most patients and at a small proportion of the cost.**

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scopic tube<sup>6,7</sup> or expandable metal<sup>8</sup> placement and repeated dilatation<sup>9</sup> are palliative and are associated with complications. Bipolar electrocautery probes may be used to recanalise the oesophagus but this technique is not widely used in the United Kingdom.<sup>10–12</sup>

Comparison of polidocanol injection with laser in the treatment of malignant oesophageal strictures showed little difference between the two techniques.<sup>13</sup> Ethanol induced tumour necrosis (ETN) was first described for the treatment of gastric carcinoma in 1984,<sup>14</sup> and was reported in the treatment of malignant dysphagia in 1987.<sup>15,16</sup> The aim of this paper is to report a larger series including the relevant technical data omitted in the initial report.

### Patients

Thirty two patients (24 male) median age 74 years (range 43–93) with inoperable, unresectable or recurrent oesophagogastric carcinoma were referred for ethanol induced tumour necrosis between 1987 and 1992. All the patients were ineligible for palliative or curative surgery, on the basis of clinical, endoscopic, and radiological (including computed tomography) assessment.

### Methods

#### ETHANOL INDUCED TUMOUR NECROSIS (ETN)

Patients attended for endoscopy after an overnight fast and were sedated with intravenous pethidine (25–50 mg) and midazolam (2–10 mg). Endoscopy was performed using a forward viewing endoscope (Olympus GIF IT20 or Q200). If the stricture was traversed easily, its anatomy and length were recorded. The stomach and duodenum were examined to exclude coexistent upper gastrointestinal disease. The endoscope was then slowly withdrawn. Aliquots of 0.5–1 ml of 100% ethanol were injected under direct vision into the tumour in a distal to proximal direction using a standard variceal injector assembly. The volume of ethanol injected during one session was left to the judgement of the endoscopist. ETN was continued until all visible tumour was injected. Successful injection was usually followed by blanching of the tumour mass. Deliberate injection into normal oesophageal mucosa was avoided. The patients had nothing by mouth and were observed for six

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Progressive dysphagia in patients with oesophagogastric carcinoma is a very distressing symptom, which can cause malnutrition and shorten life. Patients are grateful for the relief that the palliation of dysphagia provides. Despite the availability of numerous treatments, prognosis of malignant oesophagogastric disease remains very poor.<sup>1</sup> Surgery can cure a few patients and palliate more, but carries substantial mortality and morbidity even in experienced hands in resectable tumours.<sup>2</sup> The natural history of the disease may be modified by radiotherapy (except in adenocarcinomas<sup>3</sup>), but its effect on dysphagia is similar to other methods of palliation.<sup>4</sup> Randomised trials of chemotherapy with cisplatin and fluorouracil combined with surgery are underway.<sup>5</sup> All other treatments, such as endo-

TABLE I Dysphagia grading system

Grade	Degree of dysphagia
0	Normal swallowing
1	Occasional sticking of solids
2	Swallows semisolid/pureed diet
3	Swallows only liquids
4	Unable to swallow saliva

TABLE II Summary of results

	Median	(Range)
Dysphagia grade before treatment	3	(2-4)
after first treatment	1	(0-3)*
best grade achieved	1	(0-3)†
Number of treatments to reach best grade	1	(1-3)
Number of dilatations/patient	1	(0-5)
Intervals between treatments (days)	28.5	(4-170)
Volume of ethanol (ml) injected/treatment	10	(1.5-29)
Survival after first treatment (days) n=26	93	(6-660)

\*=p<0.005, †=p<0.003 Wilcoxon rank sum test.

hours after the procedure. A chest x ray was obtained and if there was no evidence of a perforation the patient was allowed liquids and discharged home with advice to start a soft diet the next day.

If the endoscope could not traverse the stricture, a guide wire was passed and the stricture dilated to only 12 mm using a bougie or balloon. The limited dilatation was to permit the endoscope to traverse the stricture. Once this was achieved ETN was done as described above.

If the lumen was totally occluded, so that a guide wire could not be passed, the proximal occluding part of the tumour was injected circumferentially, with a further endoscopy 3-7 days later. If a lumen was still not visible, further circumferential injection was done. This process was repeated at intervals of 3-7 days until a lumen was present.

To achieve initial oesophageal recanalisation and good relief of dysphagia some patients required a course (more than one treatment session) of ETN. The interval between treatment

sessions was 3-7 days. During this initial course of ETN, hospital admission was desirable in frail patients. After discharge from hospital, patients developing further dysphagia were asked to contact the endoscopy unit to arrange further treatment.

GRADING OF DYSPHAGIA

Dysphagia was graded using a system similar to that used by Bown *et al*<sup>17</sup> (Table I). Scoring of dysphagia was done by the endoscopist immediately before, and three days after each treatment session. The significance of changes in dysphagia grade after ETN was assessed by the Wilcoxon rank sum test for paired non-parametric data.

The endoscopist provided a full verbal explanation of the procedure to the patients before treatment. All patients gave written consent.

Results

The procedure was well tolerated and no patient needed additional analgesia afterwards. There were no procedure related complications.

Thirty two patients (24 male) were treated. Their median age was 74 years (range 43-93). Twenty three patients were inoperable, five had tumours judged unresectable at surgery and in four patients tumours had recurred after previous operations. Twenty three patients had adenocarcinomas, eight had squamous cell carcinomas, and one patient had a small cell carcinoma.

Each patient needed 1 (1-3) median (range) treatment sessions of ETN to achieve best dysphagia grade (Table II). The volume of ethanol injected during each treatment session was 10 ml (1.5-29) median (range).

Fourteen patients required stricture dilatation to 12 mm before ETN (Figs 1 and 2). In these patients, the improvement in dysphagia achieved was similar to patients who did not need dilatation, suggesting that the improvement in dysphagia was not due to dilatation.

In six patients with total occlusion of the oesophagus, injection of alcohol into proximal tumour was performed. Recanalisation was achieved in all six patients with no patient requiring more than three treatment sessions.

Figures 3A and 3B (endoscopic views) show successful recanalisation of a tumour occluded oesophagus in a patient before and one week after ETN.

Figure 4A (radiographs) shows a malignant oesophageal stricture and Fig 4B shows the same patient one year later; after four sessions of ETN with the oesophageal lumen still patent.

Figures 1 and 2 show individual patient responses to ETN. Figure 1 compares pretreatment dysphagia grade with the dysphagia grade after one treatment. The median dysphagia grade improved from 3 pretreatment (able to swallow liquids only) to 1 after treatment (occasional sticking of solids). Figure 2 compares pretreatment dysphagia grade with the best dysphagia grade achieved usually after an initial course (1-3 treatment sessions) of ETN.

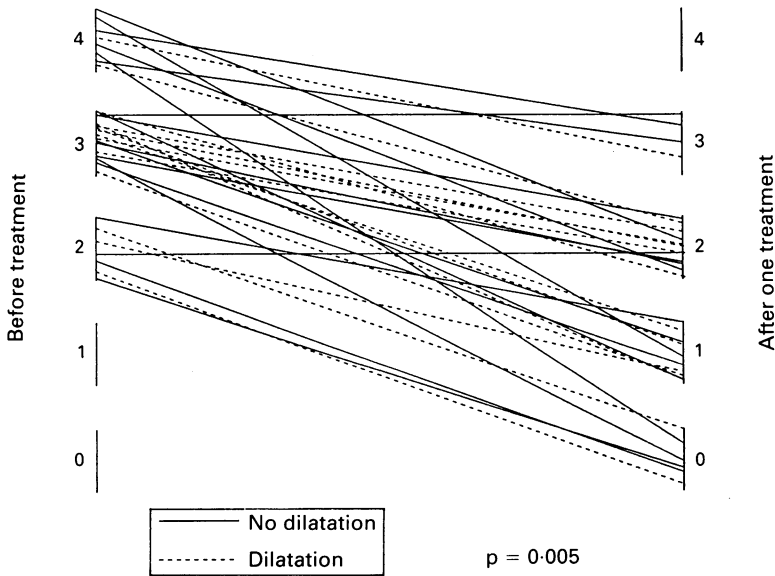


Figure 1: Response to ethanol induced tumour necrosis (ETN) in individual patients: before treatment dysphagia grade (left vertical axis) is compared with dysphagia grade after one ETN treatment session (right vertical axis).

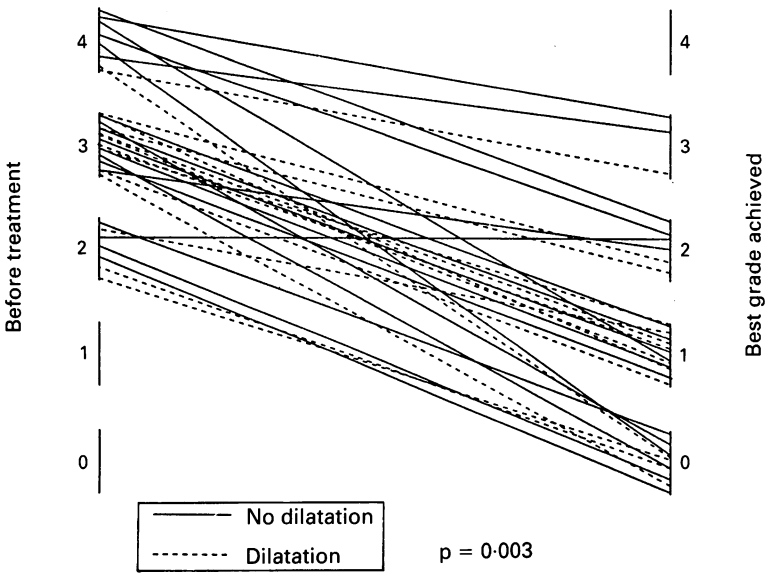


Figure 2: Response to ETN in individual patients: before treatment dysphagia grade (left vertical axis) is compared with best dysphagia grade achieved (right vertical axis) after one to three ETN treatments.

After ETN, most patients with severe dysphagia could eat a normal diet with occasional sticking of solids and 10 patients were rendered completely free of dysphagia. For one patient dysphagia failed to improve despite endoscopic evidence of oesophageal recanalisation. Fibrotic tumours, especially those recurring in anastomoses, proved more resistant to ETN, but responded to repeated treatment.

Twenty six patients had died at the time of the preparation of this paper. Median survival after first treatment was 93 days (range 6–660) (Table II). Relief of dysphagia could be maintained until death with a median interval between treatments of 28.5 days.

Discussion

Provided the tumour is resectable surgery probably provides the best palliation in patients with malignant dysphagia, even in those in whom hope for cure is unrealistic. Cunha-Melo and Earlam in a retrospective analysis of 83 000 cases of oesophageal cancer suggest that resection (curative or palliative) is only possible in 39% of

patients.<sup>18</sup> Moreover, morbidity and mortality, even in skilled hands is considerable.<sup>2</sup> The patients in our study were assessed by a dedicated oesophageal surgeon and found to be either unfit for surgery and therefore inoperable, or have unresectable or recurrent disease.

Recanalisation of the oesophagus with ND-YAG laser offers good palliation,<sup>4 12 13 17 19 20</sup> but the capital outlay needed is out of the reach of many district general hospitals. Patients with grim prognoses and a limited life expectancy may be compelled to travel long distances to a centre with endoscopic laser facilities to receive treatment that often has to be performed more than once. ETN requires no additional investment in a unit already offering sclerotherapy for bleeding oesophageal varices. Most patients can be treated as day cases, but should be able to 'self refer' themselves immediately for further treatment, if dysphagia recurs. Frail patients needing a course of ETN may require a short in hospital stay.

Laser recanalisation of the oesophagus may be complicated by perforation in 2–6% of cases.<sup>17 20</sup> We have had no procedure related complications and limited dilatation to 12 mm diameter may have contributed to this. Partial dilatation permits the endoscope to traverse the stricture, so that ETN can be done safely and effectively. As with laser, a totally occluded oesophagus may be recanalised successfully in several ETN treatment sessions by injecting alcohol into the proximal tumour. ETN shares the advantage of laser as it can deal with tumours in the cervical oesophagus. As with laser, however, tumours in the region of the cricopharyngeus present a special problem as the endoscope may not enter the proximal oesophagus to allow ETN to be performed safely. No difficulties were experienced with tumours located in other parts of the oesophagus.

Most of our patients presented with severe dysphagia but after treatment were able to eat normally with occasional sticking of solids. They were not restricted to a pureed diet, which is needed in patients treated by endoscopic intubation.<sup>6 7</sup> Although no objective assessment of quality of life was made, most patients reported relief and satisfaction with their treatment. The median improvement in dysphagia grade in our patients was 2.0. Using a similar grading system, Bown *et al* reported a 'mean' improvement of 1.7

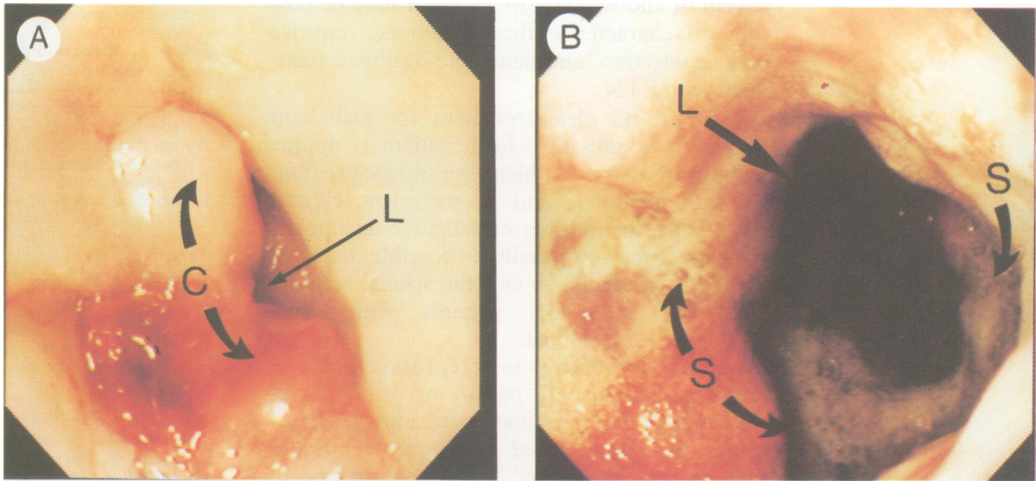


Figure 3: (A) Endoscopic view of a carcinoma (C) occluding the oesophagus, before ETN. The lumen (L) is obliterated. The patient had grade 4 dysphagia; (B) endoscopic view of the oesophagus in the same patient seven days after one ETN session. The tumour is recanalised leaving areas of ulceration and slough (S) and a patent lumen (L). Swallowing reverted to normal (dysphagia grade 0).

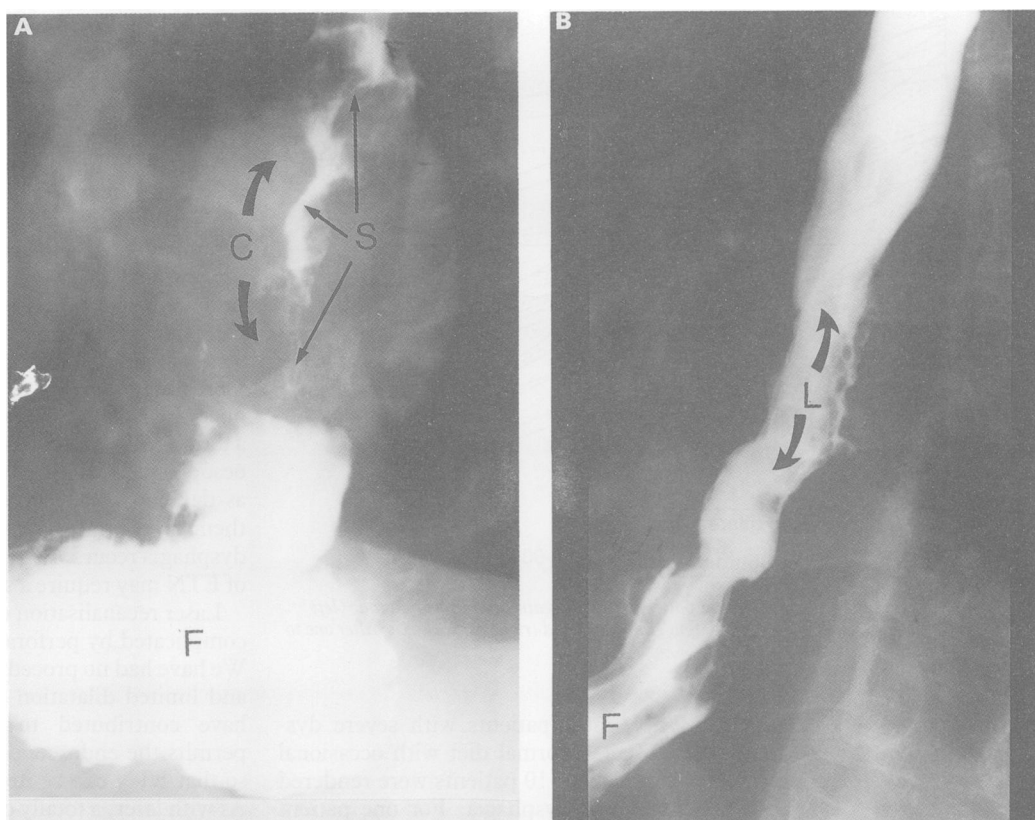


Figure 4: (A) Barium radiograph showing an oesophageal carcinoma (C) in a patient presenting with grade 3 dysphagia before ETN. There is a tight stricture (S) in the distal oesophagus. (F denotes fundus of stomach); (B) the same patient one year later after four ETN sessions. There is a wide patent lumen (L). The patient's dysphagia improved to and remained at grade 1.

in patients treated by laser.<sup>17</sup> No comparative studies have been reported.

The longest survivor in this study lived for 660 days after initial treatment with ETN (Figs 1 and 2). He presented initially with grade 4 dysphagia. In the 660 days, he had seven sessions of ETN and was maintained with virtually no dysphagia and a reasonable quality of life until he died with pulmonary metastases, showing that luminal growth can be controlled for long periods. Severe cardiopulmonary disease with known metastases had precluded surgery as an initial treatment option.

Although there are no comparative studies, there seems to be little difference in the results of ETN and Nd-YAG laser. A few fibrous tumours respond poorly to ETN and are probably best treated by endoscopic intubation. With the advent of endoscopic ultrasound it may be possible to characterise these tumours, improve patient selection, and hence the results of treatment with ETN.

There is no ideal treatment for malignant dysphagia at present.<sup>21</sup> Each patient is unique with regard to tumour histology and localisation, stricture anatomy, and pretreatment clinical state. With the number of palliative techniques available it may eventually be possible to design treatment strategies to suit the special requirements of individual patients with oesophagogastric carcinoma.

Another approach is to accept the efficacy of existing methods of palliation,<sup>22</sup> and direct studies at testing combinations of adjuvant treatments with established palliation techniques such as brachytherapy<sup>23,24</sup> and external beam

radiotherapy.<sup>25,26</sup> These combinations should be aimed at modifying disease and controlling tumour bulk. ETN has all the hallmarks of a good palliative technique being safe, inexpensive, and readily available; bringing palliation to the patients' 'doorstep'. It controls tumour bulk effectively. The next step should be the addition of a disease modifying technique, for example brachytherapy, with the object of decreasing the number of treatments needed to maintain prolonged oesophageal patency.

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